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EXAMINER
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FOSTER, CHRISTINE E

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1641

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/711,517	<b>Applicant(s)</b> ABBOTT ET AL.	
	<b>Examiner</b> Christine Foster	<b>Art Unit</b> 1641	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 19 September 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-41 is/are pending in the application.
- 4a) Of the above claim(s) 24-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☒ Claim(s) 3,9,11 and 13 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 9/23/04 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Notice to Comply</u> .                 |

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of Group I, claims 1-23 in the reply filed on 9/19/05 is acknowledged. The traversal is on the ground(s) that no undue burden is placed on the examiner to search and examine all claims, and in particular with regard to examination of products and processes for their use, for example Groups I and II. Applicant also traverses on the grounds that the processes of Groups I and III and the products of Groups II and IV are related. This is not found persuasive because the record as clearly set forth in the previous office action indicates that Inventions I-IV are patentably distinct inventions with different classification that would require non-coextensive searches (see the previous office action, pages 2-4 and item 6 in particular).

Applicant has requested rejoinder of claims 24-41 with claims 1-23. Because Applicant has elected process claims for prosecution, the withdrawn claims are not subject to rejoinder. Conditions for possible rejoinder were set forth in item 8 of the previous office action.

The requirement is still deemed proper and is therefore made FINAL.

Claims 24-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

***Information Disclosure Statement***

An Information Disclosure Statement (IDS) has not been received. The Examiner notes that submission of an IDS is not required, but reminds Applicant of the duty to disclose information material to patentability (see MPEP § 1.56).

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

***Specification***

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

**Specifically, it is noted that page 69 of the specification discloses amino acid sequences identified by SEQ ID Nos (paragraph 197). However, neither a paper copy of the sequence listing nor a computer readable form has been submitted.**

Applicant is given ONE MONTH, or THIRTY DAYS, whichever is longer, from the mailing date of this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825.

Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

The use of the trademark "Adobe Photoshop" has been noted in this application (paragraph 188). It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

### ***Drawings***

The drawings are objected to because: In Figures 1.2, 4.2, and 6.2, portions of the text are unreadable.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure

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must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

### ***Claim Objections***

Claims 3, 9, 11 and 13 are objected to because of the following informalities:

Claim 3 recites "antibodies or functional fragment thereof". It is suggested that "fragment" be pluralized since "antibodies" appears in the plural.

Claim 9 has an extra space in the words "antibody-terminated".

Claim 11 appears to require an article such as "the" prior to "amount".

Claim 13 is grammatically incorrect in that it appears to require the word "and" before "further".

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim recites a method wherein contacting the affinity substrate with a detection surface is performed on at least a partially curved affinity substrate. This “partially curved affinity substrate” would seem to include affinity substrates in which a portion of the substrate is curved, as well as substrates in which the entire substrate is curved to some partial degree. It would also include substrates curved through the manufacturing process as well as those that become curved throughout the performance of the method of the claimed invention. However, the particular type of “partially curved affinity substrate” is not specifically disclosed. The specification discloses that “The method comprises the steps of: (a) contacting the ligand to a first surface, wherein the ligand is at least in part attached to the first surface; (b) contacting the ligand-decorated first surface to a second surface, wherein the ligand is at least in part attached to the second surface, such that at least a portion of the first surface is partially curved.” It would therefore seem from this description that at least a portion of the affinity substrate is partially curved as a result of steps (a) and (b). There is no description of manufacture of curved substrates.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
3. Claim 1 recites “inking” and “stamping” in parentheses in lines 3 and 5 of the claim. The parenthetical terms render the claim indefinite, as it is unclear what the terms refer to in the claim. It is also unclear whether the parenthetical terms are meant to define the preceding words or to provide an example of same.
4. Claim 1 recites the limitation "the ligand which is bound to the receptor" in part (b). There is insufficient antecedent basis for this limitation in the claim. Part (a) recites that the receptor is *capable of* binding to the ligand, but the claim does not recite a step in which the ligand *is* bound to the receptor.
5. Claim 1 is rejected as vague and indefinite because the claim recites “detecting presence of the ligand on the detection surface” in step (c) but does not how the ligand is detected on the liquid crystal detection surface.
6. Claim 1 recites that the detection surface “further comprises a liquid crystal” in part (c). The claim is indefinite because this would imply that the detection surface comprises a liquid crystal when it is contacted with the affinity substrate, yet the specification discloses that “[t]ypically, the liquid crystal is placed on the detection surface after it has been contacted with the affinity substrate” (p. 15).
7. Claim 2 recites the limitation "the detection substrate" in part (e). There is insufficient antecedent basis for this limitation in the claim. Claim 1 recites a “detection surface”.



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8. Claim 3 recites “antibodies or functional fragment thereof”. The term “functional fragment thereof” is indefinite because it is unclear what function(s) are preserved in the fragments.
9. Claim 3 recites “nucleic acid analogs or mimic”. It is unclear what chemical structures would be considered a nucleic acid “analog” or “mimic” as the terms are not defined in the specification.
10. Claim 3 recites a Markush group terminated with “or a fragment thereof”. It is unclear whether “a fragment thereof” refers to fragments of only the last member of the Markush group (a herbicide) or to fragments all of the Markush group members. The term is also indefinite, because the specification does not provide specific disclosure of “fragments” of herbicides, viruses, mammalian cells, etc., such that one skilled in the art would not be reasonably apprised of the scope of the invention. It is unclear what compound(s) would be considered “fragments” of the recited members for use according to the method of the invention.
11. Claim 6 recites a method wherein PDMS is “peptide-terminated”. It is unclear what is meant by “peptide-terminated”. Is the peptide the receptor in this instance? Is the peptide attached to PDMS?
12. Claims 7 and 9 recite a method wherein a species is “capable of detecting” a phosphorylated peptide (claim 7) or a protein (claim 9). The claim is indefinite because it would appear that the detected species would correspond to the “ligands” recited in claim 1, but this is not explicitly stated. With regard to claim 7, it is further unclear whether the capability of detecting relates to the “method for detecting a ligand” of claim 1, or whether a separate step or functionality of detecting is referred to.

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13. Claim 7 is also rejected as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the specification discloses that peptide-terminated PDMS stamps are used to detect phosphorylated peptides by contacting the peptide-terminated stamp with phosphospecific antibodies (see paragraph 197). As there is no disclosure of any other means by which peptide-terminated PDMS may be capable of detecting phosphorylated protein, the phosphospecific antibodies are an essential element that is omitted from the claims.

14. Claim 8 recites “antibody-terminated” PDMS. It is unclear how PDMS is terminated by an antibody, as discussed above.

15. Claim 13 recites receptors that have specificities for more than one ligand. It is unclear whether the receptors are of a single type, and have dual specificity (for example) for two ligands, or whether an array of different types of receptors is immobilized, such that different types of receptors have specificity for different types of ligands. It is also unclear whether “more than one ligand” refers to molecules of a single type of ligand, or to different types of ligand.

16. Claim 14 recites receptors capable of detecting phosphorylation at “various residues” of EGFR. It is unclear what “various residues” are referred to.

17. Claim 18 recites a partially curved affinity substrate. The term “partially curved affinity substrate” is indefinite because the specification discloses that “The method comprises the steps of: (a) contacting the ligand to a first surface, wherein the ligand is at least in part attached to the first surface; (b) contacting the ligand-decorated first surface to a second surface, wherein the ligand is at least in part attached to the second surface, such that at least a portion of the first surface is partially curved.” It would therefore seem from this description that at least a portion

of the affinity substrate is partially curved as a result of steps (a) and (b). However, the claim language suggests that the affinity substrate is inherently curved. It is also unclear whether “partially” refers to a part of the affinity substrate or to partial curvature.

18. Claim 18 also recites “a detection surface”. It is unclear whether this is the same detection surface as recited in claim 1, or a different surface.

19. Claim 23 recites the limitation "the orientation". There is insufficient antecedent basis for this limitation in the claim.

### *Claim Rejections - 35 USC § 103*

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

21. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

22. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

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evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

23. Claims 1-5, 8-13, 15-20 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. ("Affinity capture of proteins from solution and their dissociation by contact printing" (2001) *Nature Biotechnology* 19:866-869) in view of Abbott et al. (US Patent No. 6,852,285 B2, previously published January 10, 2002 as US 2002/0004216).

Bernard et al. teach a method for detecting a ligand comprising (a) contacting a sample having a ligand (e.g., <sup>125</sup>I-IgG in PBS containing 10% fetal calf serum) with an affinity substrate (polydimethylsiloxane (PDMS) stamp), wherein the affinity substrate comprises a receptor capable of specifically binding the ligand (anti-mouse IgG) (see Figures 1-2 p. 866, in particular the abstract, left column, and the first paragraph of "Results and Discussion"). Bernard et al. further teach (b) contacting the PDMS stamp with a detection surface (glass or polystyrene), wherein at least a portion of the ligand which is bound to the receptor is transferred to the detection surface (see in particular p. 866, left column, second paragraph, and the first paragraph of "Results and Discussion"; p. 869, "Affinity stamping").

Bernard et al. fail to teach that the detection surface that further comprises a liquid crystal.

Abbott et al. teach a method for detecting a ligand comprising contacting a ligand with a detection surface ("substrate"), wherein at least a portion of the ligand is transferred to the detection surface, and detecting the presence of the ligand on the detection surface ("substrate"),

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wherein the detection surface comprises a liquid crystal (see column 5, lines 29-35 and line 62 to column 6, line 1-5; column 13, lines 15-21; column 13, lines 7-35; column 14, lines 20-47). In particular, Abbott et al. teach liquid crystal devices comprising one or more substrates for detection of ligand (“analyte”), wherein the ligand is contacted with a substrate that contains a receptor (“recognition moiety”) for the analyte as well as a liquid crystal (mesogens), which undergo a detectable switch in orientation upon interaction of the ligand and receptor, allowing for the ligand to be detected. The use of liquid crystals in the detection surface of Abbott et al. obviates the need for prelabeling of ligand, such as with a radiolabel or a fluorescent moiety (see column 5, lines 7-12).

With regard to claim 2, Bernard et al. teach washing the affinity substrate after the inking step (a) above (p. 869, “Affinity stamping”).

With regard to claims 4-5, Bernard et al. teach affinity substrates consisting of PDMS as an inert elastomer (p. 866, left column, paragraph 3).

With regard to claims 8-9, the PDMS affinity substrates of Bernard et al. would seem to be “antibody-terminated” because the antibodies are attached to the ends of PDMS stamps (Figure 1). The antibodies are capable of detecting a protein ( $^{125}\text{I}$ -IgG). Bernard et al. teach the use of antibodies in this context as capturing molecules (e.g., see p. 866, first two paragraphs of “Results and Discussion”).

With regard to claim 10, the antibodies, protein A, and streptavidin were applied to the affinity stamps via the cross-linker BS3 (p. 869, “Derivatization of stamps”).

With regard to claim 11, while not specifically recited, the amount of ligand present in the sample was inherently quantified because Bernard et al. teach the concentrations of the

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ligands TRITC-labeled rabbit IgG and biotinylated alkaline phosphatase in the samples (see p 869, “Affinity Stamping”).

With regard to claims 12-13, Bernard et al. (as noted above) teach that the PDMS stamp may be patterned with arrayed capturing sites with various types of receptors for screening several analytes in a parallel manner (p. 868, right column). One skilled in the art would immediately envisage that “various types of receptors” would mean receptors that have specificities for different ligands. It is also noted that Bernard et al. teach a stamp with distinct locations in the form of a surface relief of parallel lines spaced evenly apart (p. 868, left column, the third full paragraph and Figure 4D in particular). It would also seem that the teeth of the PDMS stamps comprise distinct locations on which arrays of receptors are located (Figure 2A). Abbott et al. teaches that the liquid crystal detection surface is capable of detecting the presence of more than one ligand, such as by using combinatorial library of compounds (see column 37, line 62 to column 38, line 22).

With regard to claims 15-17, Abbott et al. further teach that the detection surface may comprise self-assembled monolayers in order to anchor the liquid crystal mesogenic layer, where the self-assembled monolayers may be formed from alkanethiols or organosulfur compounds and may comprise amines through functionalization (the abstract; column 19, lines 32-42 and column 20, lines 1-7). Abbott et al. teach that the detection surface may be treated with 1-aminododecanoic acid to make the surface surface-active (column 25, lines 30-35). With regard to claim 19, Abbott et al. teach that use of certain self-assembled monolayers enables homeotropically anchoring of mesogens (column 19, lines 36-40 and column 12, lines 62-64 in particular).

With regard to claim 18, the specification discloses that “The method comprises the steps of: (a) contacting the ligand to a first surface, wherein the ligand is at least in part attached to the first surface; (b) contacting the ligand-decorated first surface to a second surface, wherein the ligand is at least in part attached to the second surface, *such that at least a portion of the first surface is partially curved*” (paragraph 28, emphasis added). Because Bernard et al. teach steps (a) and (b) as recited in the passage above, it would seem that the affinity substrate of Bernard et al. meets this limitation since the specification discloses no specific structural limitations associated with a partially curved surface, but rather indicates that the partial curvature is merely a result or conclusion of the steps above.

With regard to claims 20 and 22, the liquid crystal mesogens of Abbott et al. may be thermotropic or lyotropic and may be nematic, chiral nematic, smectic, frustrated liquid crystals, or discotic liquid crystals (column 30, line 33 to column 32, line 29), and a preferred liquid crystal is 4-cyano-4'-pentylbiphenyl (5CB) (column 37, lines 57-61).

With regard to claim 23, Abbott et al. teach that the detection surface allows for optical detection of orientation of the liquid crystal (mesogens) (the abstract and column 5, lines 15-26), and further teaches that optical output allows for ease of detection (column 5, lines 15-19).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the method for detecting a ligand of Bernard et al. using the detection surface of Abbott et al., because Abbott et al. teach that liquid crystal detection surfaces do not require labeling of the ligand as was performed in Bernard et al. One would have reasonable expectation of success in affinity stamping the surface of Abbott et al. according to the method of Bernard et al. because

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the surface of Abbott et al. is compatible with stamping by microcontact printing (see column 17, lines 5-22).

24. Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. in view of Abbott et al. as applied to claims 1 and 5 above, and further in view of Houseman et al. ("Maleimide-Functionalized Self-Assembled Monolayers for the Preparation of Peptide and Carbohydrate Biochips" (2003) *Langmuir* 19:1522-1531, Published on Web 11/13/2002).

Bernard et al. and Abbott et al. are as discussed above. Bernard et al. teaches a method in which the PDMS stamp is antibody-terminated, but fails to teach a method wherein PDMS is terminated with a peptide.

Houseman et al. teach peptides that may be immobilized to substrates and tested for their ability to serve as substrates for phosphorylation by a kinase (p. 1527, "Characterization of Kinase Activity"). Peptides that have been successfully phosphorylated are then detected by binding to phosphotyrosine-specific antibody.

It would have been obvious to employ peptides immobilized to substrates and react them with kinases, as taught by Houseman et al., as the capturing molecules (receptors) in the method of Bernard et al. in order to characterize kinase activity and establish whether the peptides are substrates of kinases. Peptides that are phosphorylated would then be capable of interacting with phosphotyrosine-specific antibody, as taught by Houseman, such that the phosphorylated peptide-terminated PDMS stamp could be inked with the phosphotyrosine-specific antibody (ligand) according to the method of Bernard et al. Detection of the phosphotyrosine-specific antibody stamped onto the surface of Abbott et al. could therefore be detected to detect the



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phosphorylated peptide. One would have a reasonable expectation of success because Bernard et al. teach that “[a]ny type of ligand-analyte interaction may be exploited” (p. 868, right column).

25. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. in view of Abbott et al. as applied to claims 1 and 12 above, and further in view of Tang et al. (US Patent No. 5,886,195).

As discussed above, Bernard et al. teaches PDMS stamps that may comprise various receptors. The liquid crystal detection surface of Abbott et al. is capable of detecting the presence of more than one ligand. However Bernard et al. and Abbott et al. do not teach a method wherein the receptors are capable of detecting the presence of protein phosphorylation at various residues of EGFR.

Tang et al. teach anti-phosphotyrosine antibodies, which may be used to measure autophosphorylation of EGFR and thereby an increase in EGF activity (column 6, lines 53-65).

Therefore, it would have been obvious to one of ordinary skill in the art to employ anti-phosphotyrosine antibodies as the capturing molecules on the PDMS stamp in the method for detecting a ligand of Bernard et al. and Abbott et al. in order to measure autophosphorylation of EGFR. One would have reasonable expectation of success because Bernard et al. teach the use of antibodies as capture molecules on PDMS stamps.

26. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. in view of Abbott et al. as applied to claim 1 above, and further in view of Tarlov et al. (“UV Photopatterning of Alkanethiolate Monolayers Self-Assembled on Gold and Silver” (1993) *J. Am. Chem. SOC.* 115, 5305-5306).

Bernard et al. and Abbott et al. are as discussed above, which fail to treat a method wherein a liquid crystal is pretreated by illumination with UV light.

Tarlov et al. teaches UV photopatterning of self-assembled monolayers on gold and silver (p. 5305, in particular the paragraph bridging the left and right columns).

It would have been obvious to pretreat the liquid crystal detection surface of Abbott et al. with UV light, as taught by Tarlov et al., in order to pattern the surface because Abbott et al. teach that the surface may be patterned by various techniques in order to produce patterns such as adjacent wells (see column 13, lines 5-64). One would have a reasonable expectation of success in employing the UV patterning method of Tarlov because Tarlov teaches patterning of alkanethiol monolayers on gold, which are embodiments also taught by Abbott et al.

### ***Conclusion***

No claims are allowed.

The following references are cited by the examiner as prior art of relevance:

Biebuyck et al. (US Patent No. 6,096,386) teach microcontact printing methods for depositing ligands on a substrate, comprising contacting a sample having or suspected of having the ligand with an affinity substrate (inking), wherein the affinity substrate comprises a receptor capable of specifically binding to the ligand (see the abstract; Figure 1; column 5, lines 15-30; column 6, lines 53-58; column 4, lines 42-50). Biebuyck et al. further teach that after the affinity substrate ("stamping means") is inked to form a ligand-receptor complex, the affinity substrate is then contacted with a detection surface ("substrate") (Figure 2; column 6, lines 53-58; column 7, lines 50-51 and column 8, lines 4-14). Biebuyck et al. teach a number of benefits to the use of

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such affinity substrates or stamping means (column 3, lines 14-62; column 4, lines 5-17): for example, by using such an affinity substrate, a number of ligands can be transferred in parallel to a substrate. Furthermore, a patterned transfer of ligands to the detection surface (substrate) may be made without needing to pattern the detection surface itself. The stamping means can be re-used, making the method very economic. Also, the stamping means and the substrate can be manufactured separately.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Christine Foster, Ph.D.  
Patent Examiner  
Art Unit 1641



LONG V. LE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600

11/14/05